Remarks

Claims 1-120 were pending in the application. Applicants added claim 121. The Office withdrew claims 32-120 from consideration. Claims 32-120 are drawn to non-elected subject matter. For ease of consideration, Applicants canceled withdrawn claims 32-120. Applicants will file divisional applications with claims reciting the non-elected subject matter of claims 32-120 in due course. Therefore, claims 1-31 and 121 are before the Office for substantive examination.

§112, Second Paragraph

The Office rejected claims 1-31 under §112, second paragraph. The Office maintains that the term "sealant" and its relation to the claimed apparatus is unclear. Applicants respectfully traverse the Office's position. The term "sealant" has a known meaning in the art. Typically, a sealant is defined in terms of 'sealing' something.[1] In this instance the sealant is used to seal non-occupied pores in the substrate to maintain the required electrophysiological gradients across the cell membranes. The term sealant and its relationship to the claimed apparatus is further described in the specification.

> The sealant material can comprise any non-conductive substance that is insoluble in the solution bathing the cells, including the polymers used to manufacture the porous layer. Preferably, the sealant comprises spun applied polyester. More preferably, the sealant layer is capable of being removed, solubilized, or made conductive at regions that contact the pores of the porous layer upon exposure to an enzyme or laser illumination. As required, the sealant layer can be selectively removed from the top, bottom, or interior of the pores that are sealed with cells. This solves the problem of open or partly open pores in the Cell Support Membrane. Notably, a sealant layer is expected to create a total Cell Support Membrane resistance of approximately one gigaohm under any given experimental conditions. To prevent the sealant

[1] "sealant." *Dictionary.com Unabridged (v 1.1)*. Random House, Inc. 23 Jan. 2007. Dictionary.com http://dictionary.reference.com/browse/sealant.

> from filling the channels of the pores, the pores can be filled with a soluble composition, such as a sugar (e.g. sucrose, maltose, etc.) composition prior to the application of the sealant layer. This filler can later be removed by incubating the Cell Support Membrane with a liquid such as water, saline solution, etc. (*See* Para. 35 of published application; page 15, line 29-page 16, line 10; *See also* page 16, lines 11-19).

Based on the plain meaning of the term "sealant" and the disclosure provided in the specification, Applicants respectfully submit that claims 1-31 comply with §112, second paragraph and the rejection should be withdrawn.

§102(b)

The Office rejected claims 1, 2 and 12-31 under §102(b) in view of Meyer *et al.* Applicants respectfully traverse the Office's position.

The Office relies on Figure 3, components 2-4, and corresponding text in Meyer to support its position. Careful inspection of Meyer leads to the conclusion that the microcuvettes described in Meyer do not teach:

> i) a first layer comprising a non-conductive material further comprising a top surface and bottom surface and including one or **more pores each extending between, and through, said top and bottom surfaces**, wherein the top surface of the material comprises one or more cell attachment sites which circumscribe each of the pores of the material and contact the cells, the pores being spaced apart such that only one pore may contact an individual cell, and wherein the pores of the material are capable of forming electrically tight seals with the contacted cells at the cell attachment sites, [emphasis added]...

Rather, Meyer appears to teach use of **closed end** microcuvettes. These microcuvettes do not comprise a **pore** extending between and through the surfaces of the substrate. Meyer provides a series of closed end, microcuvettes arranged in a planar substrate such that micropipettes can be brought into contact with cells bound to the opening of the microcuvette. A close-up view of Meyer Figure 3 confirms the same (see below).

FIG. 3

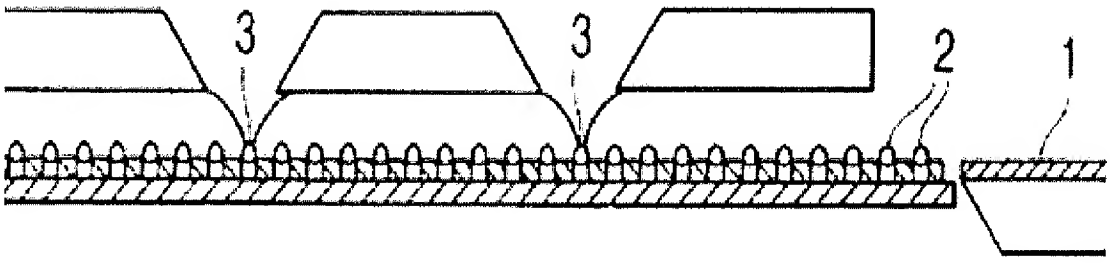
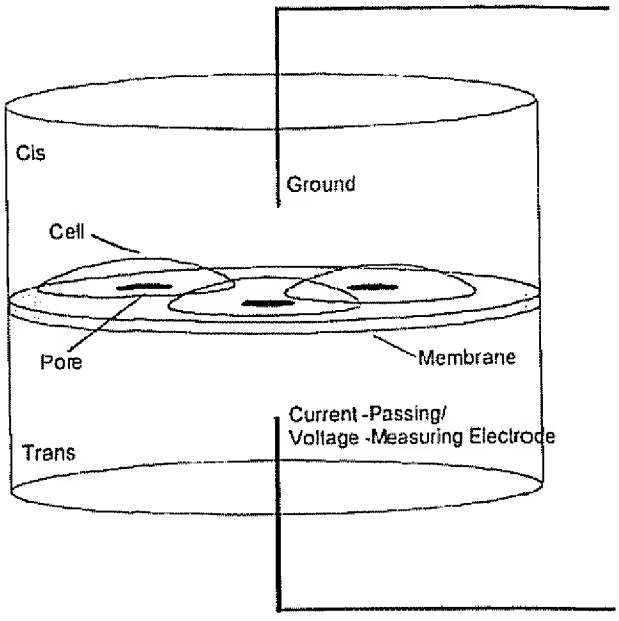


Figure 3 of Meyer shows cells (2) resting on top of the microcuvette arrangement (1) which can then be contacted with a micropipette (3). It is clear that the microcuvette arrangement (1) lack pores that extend from the "top" surface of the microcuvette arrangement (holding cell (2)) through to the "bottom" side of the microcuvette arrangement.

Contrast Meyer with the arrangement provided in Figure 1 of Applicants' disclosure. The "membrane" comprises a pore which passes **through** the membrane from the cis side to the trans side, which facilitates measurement of current across the cell bound to the pore.



There is no teaching in Meyer of a porous substrate as recited in Applicants' claims. As such, Meyer fails to describe each element of claims 1, 2, and 12-31.

§103(a)

The following summarizes the Offices' positions under §103: claim 3 was rejected in view of Meyer and Farb; claims 4-5 in view of Meyer and Shimizu; claims 8-9 in view of Meyer and Baumann; and claims 10-11 in view of Meyer and Bossuyt. Applicants traverse the Office's position for the reasons provided below.

As set forth above, Meyer fails to teach each element of claim 1 because Meyer, *inter alia*, fails to describe a porous substrate wherein the pores extend through the substrate. Given that Meyer fails to describe a porous substrate as recited in Applicants' claims (an element not found in any of the other cited references), the Office's §103 positions fail.

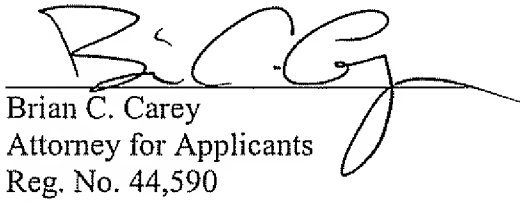
Even if Meyer taught each element of the base independent claims (which it does not), the Offices' §103 fails because the Office did not establish a *prima facie* case of obviousness. For example, critically absent from the Office's analysis is evidence or discussion of "motivation" to combine the cited references to arrive at the claimed subject matter. It is well established that "The first requirement [of an obviousness analysis] is that a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential evidentiary component of an obviousness holding.'" *CR Bard, Inc., v. M3 Sys. Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998). The Office failed to provide this essential evidentiary component and the rejection under §103 should not be maintained.

In view of the remarks made herein, Applicants respectfully submit that the claims are in condition for allowance and favorable action is, therefore, respectfully requested.

Please direct any questions concerning this Response or any aspect of this case to the undersigned attorney.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,



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